REMARKS/ARGUMENTS

Claims 32, 36, 37, 41, 55, 60, and 64 are amended to promote the clarity of the claims and to correct typographical errors. Support for the amendment can be found, e.g., at page 3, lines 7-10 of the specification and Figure 7. No new matter is added. Claims 32, 34-38, 40-45, 55, 58-61, and 63-68 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

Election/Restrictions

The Examiner requests that claim 37 be canceled, citing MPEP § 821.01. Applicants respectfully traverse.

MPEP § 821.01 requires that claims directed to non-elected inventions and not eligible for rejoinder be canceled in response to a final rejection. However, in this instant case, claim 32 is a generic claim, and claim 37, dependent from claim 32, is drawn to a non-elected species. As such, claim 37 is eligible for rejoinder once claim 32 is allowed, and therefore is not required to be canceled at this point. The Examiner's request should be withdrawn.

Claim Rejections – 35 USC § 102

Claims 32, 34, 35, 41-43, 55, 58, 59, and 64-66 are rejected as being anticipated by Alexeev et al. (Nature Biotech. 2000, 18:43-47; "Alexeeve"). Applicants respectfully traverse.

Among the rejected claims, claim 32 is the only independent claim, which will be discussed first. Claim 32, as amended, is directed to a method for inhibiting the expression of a target gene in a cell that expresses the targeted gene. The method comprises the steps of:

a) providing a composition comprising an mRNA-cDNA hybrid duplex prior to contacting said cell, wherein the mRNA-cDNA hybrid duplex is capable of inhibiting the expression of said targeted gene in said cell; and

b) contacting said cell with said composition under conditions such that the expression of said gene in said cell is inhibited.

As described in the specification, the mRNA component of the duplex is in the sense orientation. See, e.g., page 3, lines 7-10 of the specification and Figure 7.

In contrast, Alexeev discloses a chimeric oligonucleotide that contains both ribonucleotides and deoxyribonucleotides. The RNA components of this molecule, i.e., aauccaaacu and uuuccgcagu, are in the anti-sense orientation. See, e.g., Figure 1 in Alexeev. As such, Alexeev does not anticipate claim 32 because it fails to teach every limitation of claim 32.

By the same token, claims 34, 35, 41-43, 55, 58, 59, and 64-66, dependent directly or indirectly from claim 32, are neither anticipated by Alexeev. Applicants respectfully request that the rejection be withdrawn.

Claim Rejections – 35 USC § 103

Claims 32, 34, 36, 38, 40-45, 55, 58, 59, 61, and 63-68 are rejected as being unpatentable over Alexeev in view of Fire et al. (U.S. Patent No. 6,506,559; "Fire") and Bennett et al. (U.S. Patent No. 6,066,500; "Bennett"). Applicants respectfully traverse.

Among the rejected claims, claim 32 is the only independent claim, which will be discussed first. As mentioned above, claim 32 requires that the mRNA component of the mRNA-DNA hybrid duplex be in the sense orientation. Alexeev, on the other hand, requires that the RNA components of the RNA-DNA molecule be in the anti-sense orientation.

Fire discloses double-stranded RNA (dsRNA) for inhibiting expression of a target gene in a cell. See, e.g., column 4, lines 20-23 of Fire. The Examiner suggests that it would have been obvious for one skilled in the art to replace the dsRNA taught by Fire with the RNA-DNA molecule taught by Alexeev. See, e.g., the Office Action, page 5, lines 13-15. While Applicants do not concede the Examiner's suggestion, the combination of Alexeev and Fire, as suggested by the Examiner, does not add up to the present invention. More specifically, the RNA-DNA molecule taught by Alexeev contains two RNA components in the anti-sense orientation. There is no teaching whatsoever in either Alexeev or Fire that the RNA components in the RNA-DNA molecule should be changed to the sense orientation. Therefore, even if the dsRNA taught by Fire is replaced with the RNA-DNA molecule taught by Alexeev, the RNA components of the RNA-DNA molecule would remain in the anti-sense orientation. Since claim 32 requires that the mRNA component of the mRNA-DNA hybrid duplex be in the sense orientation, the combination of Alexeev and Fire, as suggested by the Examiner, not only does not render claim 32 obvious, but also teaches away from claim 32.

Bennett discloses anti-sense compounds, particularly oligonucleotides, which are targeted to a nucleic acid encoding β-catenin, and which modulate the expression of β-catenin. See, e.g., column 2, lines 56-60 of Bennett. There is no indication whatsoever in Alexeev, Fire, or Bennett that the references should be combined such that the RNA components in the RNA-DNA molecule taught by Alexeev should be changed to the sense orientation. Neither does the Examiner so suggest.

Furthermore, as described in the specification, a sense RNA-DNA hybrid has advantages over an anti-sense RNA-DNA hybrid or a dsRNA unexpected by Alexeev, Fire, and Bennett. For example, when a sense RNA-DNA hybrid, an anti-

sense RNA-DNA hybrid, and a dsRNA were each introduced into human LNCaP prostate cancer cells for bcl-2 gene interference, the sense RNA-DNA hybrid inhibited bcl-2 expression with an efficiency significantly higher than that of the anti-sense RNA-DNA hybrid or the dsRNA. See, e.g., page 16, lines 18-29 of the specification and Figure 3. A sense RNA-DNA hybrid also has advantages over an anti-sense oligonucleotide unexpected by Alexeev, Fire, and Bennett. For example, compared to an anti-sense DNA, a sense RNA-DNA hybrid showed relatively long-term initiation and maintenance in knocking out a target gene, and the concentration of the sense RNA-DNA hybrid needed for producing the biological effects was almost a half million-fold less than that of the anti-sense DNA. See, e.g., page 16, line 30 – page 17, line 3 of the specification. Without any knowledge about the advantages of a sense RNA-DNA hybrid, one skilled in the art would not have been motivated to combine Alexeev, Fire, and Bennett to come up with the present invention.

Taken together, Alexeev, Fire, and Bennett do not render claim 32 obvious because the cited references, alone or in combination, fail to teach or suggest an mRNA-DNA hybrid duplex where the mRNA component is in the sense orientation. Claim 32 is also non-obvious in view of the cited references because a sense RNA-DNA hybrid has advantages over an anti-sense RNA-DNA hybrid, a dsRNA, or an anti-sense oligonucleotide unexpected by the cited references.

By the same token, claims 34, 36, 38, 40-45, 55, 58, 59, 61, and 63-68, dependent directly or indirectly from claim 32, are also patentable over Alexeev, Fire, and Bennett. Withdrawal of the rejection is thus respectfully requested.

CONCLUSION

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

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